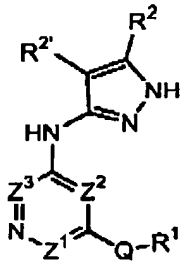
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1 (Currently amended): A compound of formula III:



III

or a pharmaceutically acceptable ~~derivative or prodrug~~ salt thereof, wherein:

Z^1 is nitrogen or CR^8, Z^2 is CH, and Z^3 is nitrogen or CR^x, provided that when one of Z^1 or Z^3 is nitrogen, the other of Z^1 or Z^3 is CR^8 or CR^x, respectively;

R^x is $T\text{-}R^3$ or $L\text{-}Z\text{-}R^3$;

Q is selected from $-N(R^4)-$, -O-, –S-, or $-CH(R^6)-$;

R^1 is T-(Ring D);

Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms selected from nitrogen, oxygen or sulfur, wherein each substitutable ring carbon of Ring D is independently substituted by oxo, $T\text{-}R^5$, or $V\text{-}Z\text{-}R^5$, and each substitutable ring nitrogen of Ring D is independently substituted by $-R^4$;

T is a valence bond or a $C_{1\text{-}4}$ alkylidene chain, wherein when Q is $-CH(R^6)-$, a methylene unit of said $C_{1\text{-}4}$ alkylidene chain is optionally replaced by -O-, -S-, $-N(R^4)-$, -CO-, -OC(O)NH-, or $-NHCO_2-$;

Z is a $C_{1\text{-}4}$ alkylidene chain;

L is -O-, -S-, -SO-, $-SO_2-$, $-N(R^6)SO_2-$, $-SO_2N(R^6)-$, $-N(R^6)-$, -CO-, $-CO_2-$, $-N(R^6)CO-$, $-N(R^6)C(O)O-$, $-N(R^6)CON(R^6)-$, $-N(R^6)SO_2N(R^6)-$, $-N(R^6)N(R^6)-$, $-C(O)N(R^6)-$, $-OC(O)N(R^6)-$, $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$,

$-C(R^6)_2N(R^6)-$, $-C(R^6)_2N(R^6)C(O)-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, or $-C(R^6)_2N(R^6)CON(R^6)-$;

R^2 and $R^{2'}$ are independently selected from -R, -T-W-R^6, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a fused, 5-8 membered, unsaturated or partially unsaturated, ring having 0-3 ring heteroatoms selected from nitrogen, oxygen, or sulfur, wherein each substitutable ring carbon of said fused ring formed by R^2 and $R^{2'}$ is independently substituted by halo, oxo, -CN, $-NO_2$, $-R^7$, or -V-R^6, and each substitutable ring nitrogen of said ring formed by R^2 and $R^{2'}$ is independently substituted by R^4;

R^3 is selected from -R, -halo, -OR, -C(=O)R, $-CO_2R$, -COCOR, $-COCH_2COR$, $-NO_2$, -CN, -S(O)R, $-S(O)_2R$, -SR, $-N(R^4)_2$, $-CON(R^7)_2$, $-SO_2N(R^7)_2$, -OC(=O)R, $-N(R^7)COR$, $-N(R^7)CO_2(C_{1-6}$ aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^7)CON(R^7)_2$, $-N(R^7)SO_2N(R^7)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^7)_2$;

each R is independently selected from hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, C_{6-10} aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms;

each R^4 is independently selected from $-R^7$, $-COR^7$, $-CO_2$(optionally substituted C_{1-6} aliphatic), $-CON(R^7)_2$, or $-SO_2R^7$;

each R^5 is independently selected from -R, halo, -OR, -C(=O)R, $-CO_2R$, -COCOR, $-NO_2$, -CN, -S(O)R, $-SO_2R$, -SR, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, -OC(=O)R, $-N(R^4)COR$, $-N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$;

V is -O-, -S-, -SO-, $-SO_2-$, $-N(R^6)SO_2-$, $-SO_2N(R^6)-$, $-N(R^6)-$, -CO-, $-CO_2-$, $-N(R^6)CO-$, $-N(R^6)C(O)O-$, $-N(R^6)CON(R^6)-$, $-N(R^6)SO_2N(R^6)-$, $-N(R^6)N(R^6)-$, $-C(O)N(R^6)-$, $-OC(O)N(R^6)-$, $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$, $-C(R^6)_2N(R^6)-$, $-C(R^6)_2N(R^6)C(O)-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, or $-C(R^6)_2N(R^6)CON(R^6)-$;

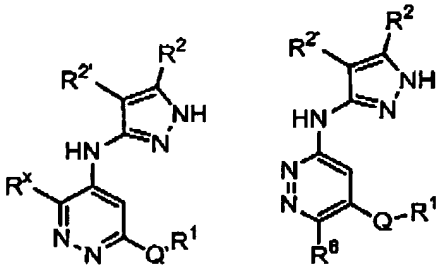
W is $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$, $-C(R^6)_2N(R^6)-$, -CO-, $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)OC(O)N(R^6)-$, $-C(R^6)_2N(R^6)CO-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, $-C(R^6)_2N(R^6)CON(R^6)-$, or $-CON(R^6)-$;

each R^6 is independently selected from hydrogen or an optionally substituted C_{1-4} aliphatic group, or two R^6 groups on the same nitrogen atom are taken together with the nitrogen atom to form a 5-6 membered heterocyclyl or heteroaryl ring;

each R^7 is independently selected from hydrogen or an optionally substituted C_{1-6} aliphatic group, or two R^7 on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring; and

R^8 is selected from -R, halo, -OR, -C(=O)R, $-CO_2R$, -COCOR, $-NO_2$, -CN, -S(O)R, $-SO_2R$, -SR, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, $-OC(=O)R$, $-N(R^4)COR$, $-N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$.

Claim 2 (Currently amended): The compound according to claim 1, wherein Q is $-N(R^4)-$, -S-, or $-CH(R^6)-$, and said compound is of formula **IIIa** or **IIIb**



IIIa **IIIb**

or a pharmaceutically acceptable ~~derivative or prodrug~~ salt thereof.

Claim 3 (Original): The compound according to claim 2, wherein said compound has one or more features selected from the group consisting of:

(a) R^x is hydrogen, alkyl- or dialkylamino, acetamido, or a C_{1-4} aliphatic group;

(b) R^1 is T-(Ring D), wherein T is a valence bond or a methylene unit;

(c) Ring D is a 5-7 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(d) R^2 is –R or –T-W-R^6 and $R^{2'}$ is hydrogen, or R^2 and $R^{2'}$ are taken together to form an optionally substituted benzo ring.

Claim 4 (Original): The compound according to claim 3, wherein:

(a) R^x is hydrogen, alkyl- or dialkylamino, acetamido, or a C_{1-4} aliphatic group;

(b) R^1 is T-(Ring D), wherein T is a valence bond or a methylene unit;

(c) Ring D is a 5-7 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(d) R^2 is –R or –T-W-R^6 and $R^{2'}$ is hydrogen, or R^2 and $R^{2'}$ are taken together to form an optionally substituted benzo ring.

Claim 5 (Original): The compound according to claim 3, wherein said compound has one or more features selected from the group consisting of:

(a) R^1 is T-(Ring D), wherein T is a valence bond, and Q is -S- or -NH-;

(b) Ring D is a 5-6 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(c) R^2 is –R and $R^{2'}$ is hydrogen, wherein R is selected from hydrogen, C_{1-6} aliphatic, phenyl, a 5-6 membered heteroaryl ring, or a 5-6 membered heterocyclic ring.

Claim 6 (Original): The compound according to claim 5, wherein:

(a) R^1 is T-(Ring D), wherein T is a valence bond, and Q is -S- or -NH-;

(b) Ring D is a 5-6 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(c) R^2 is -R and $R^{2'}$ is hydrogen, wherein R is selected from hydrogen, C_{1-6} aliphatic, phenyl, a 5-6 membered heteroaryl ring, or a 5-6 membered heterocyclic ring.

Claim 7 (Original): The compound according to claim 5, wherein said compound has one or more features selected from the group consisting of:

(a) R^x is hydrogen methyl, ethyl, propyl, cyclopropyl, isopropyl, methylamino or acetamido;

(b) R^1 is T-(Ring D), wherein T is a valence bond and Ring D is a 5-6 membered aryl or heteroaryl ring, wherein Ring D is optionally substituted with one to two groups selected from -halo, -CN, -NO_2, -$N(R^4)_2$, optionally substituted C_{1-6} aliphatic group,

-OR, -CO_2R, -$CON(R^4)_2$, -$OCO(R^4)_2$, -$N(R^4)COR$, -$N(R^4)SO_2R$,
-$N(R^5)COCH_2CH_2N(R^4)_2$, or -$N(R^6)COCH_2CH_2CH_2N(R^4)_2$; and

(c) R^2 is hydrogen or a substituted or unsubstituted C_{1-6} aliphatic.

Claim 8 (Original): The compound according to claim 7, wherein:

(a) R^x is hydrogen methyl, ethyl, propyl, cyclopropyl, isopropyl, methylamino or acetamido;

(b) R^1 is T-(Ring D), wherein T is a valence bond and Ring D is a 5-6 membered aryl or heteroaryl ring, wherein Ring D is optionally substituted with one to two groups selected from -halo, -CN, -NO_2, -$N(R^4)_2$, optionally substituted C_{1-6} aliphatic group, -OR, -CO_2R, -$CON(R^4)_2$, -$OCO(R^4)_2$, -$N(R^4)COR$, -$N(R^4)SO_2R$, -$N(R^6)COCH_2CH_2N(R^4)_2$, or -$N(R^6)COCH_2CH_2CH_2N(R^4)_2$; and

(c) R^2 is hydrogen or a substituted or unsubstituted C_{1-6} aliphatic.

Claim 9 (Previously presented): A compound selected from the group consisting of:

N^5-(1*H*-Indazol-6-yl)-N^3-(5-methyl-1*H*-pyrazol-3-yl)-pyridazine-3,5-diamine;

N-{4-[6-(5-Methyl-1*H*-pyrazol-3-ylamino)-pyridazin-4-ylsulfanyl]-phenyl}-acetamide;

[5-(3-Methoxy-benzyl)-pyridazin-3-yl]-(5-methyl-1*H*-pyrazol-3-yl)-amine;

N^3-(5-Cyclopropyl-1*H*-pyrazol-3-yl)-N^5-pyridin-3-ylmethyl-pyridazine-3,5-diamine;

[5-(Benzothiazol-6-ylsulfanyl)-pyridazin-3-yl]-(5-cyclopropyl-1*H*-pyrazol-3-yl)-amine;

{4-[6-(5-Cyclopropyl-1*H*-pyrazol-3-ylamino)-pyridazin-4-yloxy]-phenyl}-acetonitrile;

N-{4-[6-(1*H*-Indazol-3-ylamino)-pyridazin-4-ylamino]-phenyl}-methanesulfonamide;

(1*H*-Indazol-3-yl)-[5-(thiophen-2-ylmethylsulfanyl)-pyridazin-3-yl]-amine;

N^5-(5-Methyl-1*H*-pyrazol-3-yl)-N^3-pyridin-3-ylmethyl-pyridazine-3,5-diamine;

[6-(Benzothiazol-6-ylsulfanyl)-pyridazin-4-yl]-(5-methyl-1*H*-pyrazol-3-yl)-amine;

{4-[5-(5-Methyl-1*H*-pyrazol-3-ylamino)-pyridazin-3-yloxy]-phenyl}-acetonitrile;

N^5-(5-Cyclopropyl-1*H*-pyrazol-3-yl)-N^3-(1*H*-indazol-6-yl)-pyridazine-3,5-diamine;

N-{4-[5-(5-Cyclopropyl-1*H*-pyrazol-3-ylamino)-pyridazin-3-ylsulfanyl]-phenyl}-acetamide;

N^5-(1*H*-Indazol-3-yl)-N^3-(1*H*-indazol-6-yl)-pyridazine-3,5-diamine; and

(1*H*-Indazol-3-yl)-[6-(3-methoxy-phenylsulfanyl)-pyridazin-4-yl]-amine.

Claim 10 (Original): A composition comprising a compound according to any of claims 1-9, and a pharmaceutically acceptable carrier.

Claim 11 (Original): The composition according to claim 10, further comprising an additional therapeutic agent.

Claim 12 (Original): A method of inhibiting Aurora-2 or GSK-3 activity in a biological sample comprising the step of contacting said biological sample with a compound according to any one of claims 1-9.

Claim 13 (Original): A method of inhibiting Aurora-2 activity in a patient comprising the step of administering to said patient a composition according to claim 10.

Claim 14 (Original): A method of inhibiting Aurora-2 activity in a patient comprising the step of administering to said patient a composition according to claim 11.

Claim 15 (Original): A method of treating an Aurora-2-mediated disease, which method comprises administering to a patient in need of such a treatment a therapeutically effective amount of a composition according to claim 10.

Claim 16 (Original): The method according to claim 15, wherein said disease is selected from colon, breast, stomach, or ovarian cancer.

Claim 17 (Original): The method according to claim 16, wherein said method further comprises administering an additional therapeutic agent.

Claim 18 (Original): The method according to claim 17, wherein said additional therapeutic agent is a chemotherapeutic agent.

Claim 19 (Original): A method of inhibiting GSK-3 activity in a patient comprising the step of administering to said patient a composition according to claim 10.

Claim 20 (Original): A method of inhibiting GSK-3 activity in a patient comprising the step of administering to said patient a composition according to claim 11.

Claim 21 (Currently amended): A method of ~~method of~~ treating a GSK-3-mediated disease, which method comprises administering to a patient in need of such a treatment a therapeutically effective amount of a composition according to claim 10.

Claim 22 (Original): The method according to claim 21, wherein said GSK-3-mediated disease is selected from diabetes, Alzheimer's disease, Huntington's Disease, Parkinson's Disease, AIDS-associated dementia, amyotrophic lateral sclerosis (AML), multiple sclerosis (MS), schizophrenia, cardiomycete hypertrophy, reperfusion/ischemia, or baldness.

Claim 23 (Original): The method according to claim 22, wherein said GSK-3-mediated disease is diabetes.

Claim 24 (Original): A method of enhancing glycogen synthesis or lowering blood levels of glucose in a patient in need thereof, which method comprises administering to said patient a therapeutically effective amount of a composition according to claim 10.

Claim 25 (Original): A method of inhibiting the production of hyperphosphorylated Tau protein in a patient, which method comprises administering to a patient in need thereof a therapeutically effective amount of a composition according to claim 10.

Claim 26 (Original): A method of inhibiting the phosphorylation of β-catenin, which method comprises administering to a patient in need thereof a therapeutically effective amount of a composition according to claim 10.